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☐ **1:** Eur J Biochem 2000 Oct;267(20):6140-50   Related Articles, Links

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Cloning, expression and chromosomal localization of a novel human dipeptidyl peptidase (DPP) IV homolog, DPP8.

Abbott CA, Yu DM, Woollatt E, Sutherland GR, McCaughan GW, Gorrell MD.

A. W. Morrow Gastroenterology and Liver Centre, Royal Prince Alfred Hospital, Centenary Institute of Cancer Medicine and Cell Biologyand The University of Sydney, NSW, Australia. c.abbott@centenary.usyd.edu.au

Dipeptidyl peptidase (DPP) IV has roles in T-cell costimulation, chemokine biology, type-II diabetes and tumor biology. Fibroblast activation protein (FAP) has been implicated in tumor growth and cirrhosis. Here we describe DPP8, a novel human postproline dipeptidyl aminopeptidase that is homologous to DPPIV and FAP. Northern-blot hybridization showed that the tissue expression of DPP8 mRNA is ubiquitous, similar to that of DPPIV. The DPP8 gene was localized to chromosome 15q22, distinct from a closely related gene at 19p13.3 which we named DPP9. The full-length DPP8 cDNA codes for an 882-amino-acid protein that has about 27% identity and 51% similarity to DPPIV and FAP, but no transmembrane domain and no N-linked or O-linked glycosylation. Western blots and confocal microscopy of transfected COS-7 cells showed DPP8 to be a 100-kDa monomeric protein expressed in the cytoplasm. Purified recombinant DPP8 hydrolyzed the DPPIV substrates Ala-Pro, Arg-Pro and Gly-Pro. Thus recombinant DPP8 shares a postproline dipeptidyl aminopeptidase activity with DPPIV and FAP. DPP8 enzyme activity had a neutral pH optimum consistent with it being nonlysosomal. The similarities between DPP8 and DPPIV in tissue expression pattern and substrates suggests a potential role for DPP8 in T-cell activation and immune function.

MeSH Terms:
- Amino Acid Sequence
- Antigens, CD26/genetics*
- Antigens, CD26/chemistry
- Cell Line
- Chromosome Mapping

- Chromosomes, Human, Pair 15*
- Chromosomes, Human, Pair 19
- Cloning, Molecular
- Growth Substances/chemistry
- Human
- Lymphocytes/enzymology
- Molecular Sequence Data
- Monocytes/enzymology
- Recombinant Proteins/chemistry
- Recombinant Proteins/biosynthesis
- Sequence Alignment
- Sequence Homology, Amino Acid
- Serine Endopeptidases/chemistry
- Support, Non-U.S. Gov't

Substances:
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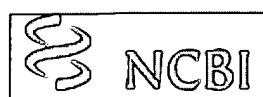- Growth Substances

Secondary source id:
- GENBANK/AF221637
- GENBANK/AF221636
- GENBANK/AF221635
- GENBANK/AF221634

PMID: 11012666 [PubMed - indexed for MEDLINE]

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☐ 1: AF221634. Homo sapiens dipe...[gi:11095187]   Links

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            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 3127)
  AUTHORS   Abbott,C.A., Yu,D.M., Woollatt,E., Sutherland,G.R., McCaughan,G.W.
            and Gorrell,M.D.
  TITLE     Cloning, expression and chromosomal localization of a novel human
            dipeptidyl peptidase (DPP) IV homolog, DPP8
  JOURNAL   Eur. J. Biochem. 267 (20), 6140-6150 (2000)
  MEDLINE   20467194
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REFERENCE   2  (bases 1 to 3127)
  AUTHORS   Abbott,C.A., Yu,D., McCaughan,G.W. and Gorrell,M.D.
  TITLE     Direct Submission
  JOURNAL   Submitted (06-JAN-2000) A.W. Morrow Gastroenterology and Liver
            Centre, Centenary Institute of Cell Biology and Cancer Medicine,
            Locked Bag No.6, Newtown, Sydney, NSW 2042, Australia
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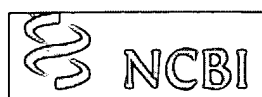
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☐ 1: AF221635. Homo sapiens dipe...[gi:11095189]   Links

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VERSION     AF221635.1  GI:11095189
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REFERENCE   1  (bases 1 to 1197)
  AUTHORS   Abbott,C.A., Yu,D.M., Woollatt,E., Sutherland,G.R., McCaughan,G.W.
            and Gorrell,M.D.
  TITLE     Cloning, expression and chromosomal localization of a novel human
            dipeptidyl peptidase (DPP) IV homolog, DPP8
  JOURNAL   Eur. J. Biochem. 267 (20), 6140-6150 (2000)
  MEDLINE   20467194
   PUBMED   11012666
REFERENCE   2  (bases 1 to 1197)
  AUTHORS   Abbott,C.A., Yu,D., McCaughan,G.W. and Gorrell,M.D.
  TITLE     Direct Submission
  JOURNAL   Submitted (06-JAN-2000) A.W. Morrow Gastroenterology and Liver
            Centre, Centenary Institute of Cell Biology and Cancer Medicine,
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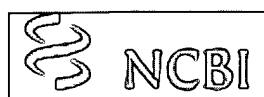
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☐ **1: AF221636. Homo sapiens dipe...[gi:11095191]**   Links

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VERSION     AF221636.1  GI:11095191
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REFERENCE   1  (bases 1 to 1669)
  AUTHORS   Abbott,C.A., Yu,D.M., Woollatt,E., Sutherland,G.R., McCaughan,G.W.
            and Gorrell,M.D.
  TITLE     Cloning, expression and chromosomal localization of a novel human
            dipeptidyl peptidase (DPP) IV homolog, DPP8
  JOURNAL   Eur. J. Biochem. 267 (20), 6140-6150 (2000)
  MEDLINE   20467194
   PUBMED   11012666
REFERENCE   2  (bases 1 to 1669)
  AUTHORS   Abbott,C.A., Yu,D., McCaughan,G.W. and Gorrell,M.D.
  TITLE     Direct Submission
  JOURNAL   Submitted (06-JAN-2000) A.W. Morrow Gastroenterology and Liver
            Centre, Centenary Institute of Cell Biology and Cancer Medicine,
            Locked Bag No.6, Newtown, Sydney, NSW 2042, Australia
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     1321 agaacattat gaactgcatc ttttgcacta ccttcaagaa aaccttggat cacgtattgc
     1381 tgctctaaaa gtgatataat tttgacctgt gtagaactct ctggtataca ctggctattt
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     1501 tgccatgtaa catctactcc tgaaaataaa tgtggtgcca tgcaggggtc tacggtttgt
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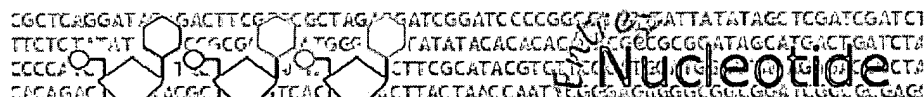
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NCBI
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Limits   Preview/Index   History   Clipboard   Details

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☐ **1: AF221637. Homo sapiens dipe...[gi:11095193]**   Links

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LOCUS       AF221637                1083 bp    mRNA    linear   PRI 05-NOV-2000
DEFINITION  Homo sapiens dipeptidyl peptidase 8 (DPP8) mRNA, partial cds,
            alternatively spliced.
ACCESSION   AF221637
VERSION     AF221637.1  GI:11095193
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 1083)
  AUTHORS   Abbott,C.A., Yu,D.M., Woollatt,E., Sutherland,G.R., McCaughan,G.W.
            and Gorrell,M.D.
  TITLE     Cloning, expression and chromosomal localization of a novel human
            dipeptidyl peptidase (DPP) IV homolog, DPP8
  JOURNAL   Eur. J. Biochem. 267 (20), 6140-6150 (2000)
  MEDLINE   20467194
   PUBMED   11012666
REFERENCE   2  (bases 1 to 1083)
  AUTHORS   Abbott,C.A., Yu,D., McCaughan,G.W. and Gorrell,M.D.
  TITLE     Direct Submission
  JOURNAL   Submitted (06-JAN-2000) A.W. Morrow Gastroenterology and Liver
            Centre, Centenary Institute of Cell Biology and Cancer Medicine,
            Locked Bag No.6, Newtown, Sydney, NSW 2042, Australia
FEATURES             Location/Qualifiers
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                     /note="serine protease; member of prolyl oligopetidase S9b
                     family belonging to enzyme clan SC; additional splice
                     variants of this mRNA are found in GenBank Accession
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                     /protein_id="AAG29769.1"
                     /db_xref="GI:11095194"
                     /translation="EEDARSAGVATFVLQEEFDRYSGYWWCPKAETTPSGGKILRILY
                     EENDESEVEIIHVTSPMLETRRADSFRYPKTGTANPKVTFKMSEIMIDAEGRIIVDEV
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HRGLKFEGAFKYKMGQIEIDDQVEGLQYLASRYDFIDLDRVGIHGWSYGGYLSLMALM
QRSDIFRVAIAGAPVTLWIFYDTGYT"

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BASE COUNT      312 a     213 c     247 g     311 t
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       61 atattctggc tattggtggt gtccaaaagc tgaaacaact cccagtggtg gtaaaattct
      121 tagaattcta tatgaagaaa atgatgaatc tgaggtggaa attattcatg ttacatcccc
      181 tatgttggaa acaaggaggg cagattcatt ccgttatcct aaaacaggta cagcaaatcc
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     1081 gga
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```

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[3.4.14.3 Transferred entry: now EC 3.4.19.1 - Acylaminoacyl-peptidase]

3.4.14.4   Dipeptidyl-peptidase III
  REACTION: Release of an N-terminal dipeptide from a peptide of four or more
      residues, with broad specificity
 OTHER NAME(S): Dipeptidyl aminopeptidase III; Dipeptidyl arylamidase III;
      Red cell angiotensinase; Enkephalinase B
  COMMENTS: A cytosolic serine-type peptidase active at neutral pH. Highly
      selective for Arg-Arg-2-naphthylamide at pH 9.2. Inactive on
      $(Glu)_4$, $(Gly)_4$, and tripeptides, as well as bonds involving
      proline
 REFERENCES: 1237, 3197, 4862

3.4.14.5   Dipeptidyl-peptidase IV
  REACTION: Release of an N-terminal dipeptide, Xaa-Xbb$\dagger$Xcc, from a
      polypeptide, preferentially when Xbb is Pro, provided Xcc is
      neither Pro nor hydroxyproline
 OTHER NAME(S): Dipeptidyl aminopeptidase IV; Xaa-Pro-dipeptidyl-aminopeptidase;
      Gly-Pro naphthylamidase; Postproline dipeptidyl aminopeptidase IV
  COMMENTS: A membrane-bound serine-type peptidase in mammals and
      flavobacteria
 REFERENCES: 2478, 3192, 5345

3.4.14.6   Dipeptidyl-dipeptidase
  REACTION: Preferential release of dipeptides from a tetrapeptide, *e.g.*
      Ala-Gly$\dagger$Ala-Gly. Acts more slowly on Ala-Ala$\dagger$Ala-Ala and
      Gly-Gly$\dagger$Gly-Gly
 OTHER NAME(S): Dipeptidyl tetrapeptide hydrolase; Dipeptidyl ligase;
      Tetrapeptide dipeptidase
  COMMENTS: A thiol-activated peptidase from cabbage (*Brassica oleracea*).
      Tetrapeptides are formed from Ala-Ala, Gly-Gly, Ala-Gly and
      Gly-Ala
 REFERENCES: 1253

[3.4.14.7 Deleted entry: Tetralysine endopeptidase]

[3.4.14.8 Transferred entry: now EC 3.4.14.9 - Tripeptidyl-peptidase I and
*   EC 3.4.14.10 - Tripeptidyl-peptidase II]*

3.4.14.9   Tripeptidyl-peptidase I
  REACTION: Release of an N-terminal tripeptide from a polypeptide
 OTHER NAME(S): Tripeptidyl aminopeptidase; Tripeptidyl peptidase
  COMMENTS: A lysosomal enzyme active at acidic pH. Inhibited by diisopropyl
      fluorophosphate. Formerly included in EC 3.4.14.8
 REFERENCES: 1111, 3194

3.4.14.10   Tripeptidyl-peptidase II
  REACTION: Release of an N-terminal tripeptide from a polypeptide
 OTHER NAME(S): Tripeptidyl aminopeptidase; Tripeptidyl peptidase
  COMMENTS: A cytosolic enzyme active at neutral pH. Inhibited by diisoprop
      fluorophosphate. Formerly included in EC 3.4.14.8
 REFERENCES: 275-6, 5066

```
DPP4    379  E.......GYRHICYFQIDKK....DCTFITKGTWEVIG....IEALTSDYLYYISNEYK
DPRP1   473  SKYKRSSGGLEAPSDFKCPIK....EEIATTSGEWEVIGRHGSNIQVDEVRRLVYFEGTK
DPRP2   464  QGYDWSEPFSPGEDEFKCPIK....EEIAITSGEWEVLARHGSKIWVNEETKLVYFEGTK
DPRP3   394  GR.....GEFHIIAMFLIQSKSEQITVRHLTSGNWEVIK....IIAYDETTQKIYFLSTE

DPP4    424  GMPGGRNLYKIQLSDYTKVTCLSCELNPERCQYYSVSFSKEAKYYQLRCSGPGLPIYTLH
DPRP1   529  DSPLEHHLYVVSYVNPGEVTRLTDRGYSHSCCISQHCDFFTSKYSNOKNP.HCVSLYKLS
DPRP2   520  DIPLEHHLYVVSYEAAGEIVRLTTPGESHSCSMSQNFDMFVSHYSSVSTP.PCVHVYKLS
DPRP3   445  SSPRGROLYSASTEGLLNRQCISCNFMKEQCIYFDASFSPMNQHFLLFCEGPRVPVVSLH

DPP4    484  SSVNDKGLRVLEDNSALDKMLQN..VQMPSKKLDFIILNETKFWYQMILPHFDKSKKYP
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DPRP2   579  GPDDDPLHNQPREWASMMEAASCPPDYMPPEIFHFHTRSDVRLYGMLYKPHALQPGKKHP
DPRP3   505  STDNPAKYFILESNSMLKEAILKKIGKF..EIKILHIDDYELPLQLSLPKDFMDRNQYA

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DPRP1   648  TVLFIYGGPQVQLVNNRFKGVKYERLNTLASLGYVVVVIDGRGSGYQGDKIMHAINRRIG
DPRP2   639  TVLFVYGGPQVQLVNNSFKGIKYLRLNTLASLGYAVVVIDGRGSCHRGLKFEGAEKYKMG
DPRP3   563  LLLIMDEEPGGQLVTDKFH..IDWDSVLIDMDNVIVARFDGRGSGFQGLKILQEIHRRLG

DPP4    600  TFEMEDQIEAARQFS.KMGFVDNKRIAIWGWSYGGYVTSMVLGSGSGVFKCGIAVAPVSR
DPRP1   708  QIEIDDQMEGLQYLASRYDFIDLDRVGIHGWSYGGYLSLMALMORSDIFRVAIAGAPVTL
DPRP2   699  QVEIEDQMEGLQFVAEKYGFIDLSRVAIHGWSYGGELSLMGLIHKPQVFKVAIAGAPVTV
DPRP3   621  SVEVKDQITAVKFLL.KLPYIDSKRLSIFGKGYGGYIASMILKSDEKLFKCGSVVAPITD

DPP4    659  WEYYDSVYTERYMGLPTPEDNLDHYRNSTVMSRAENFKQVEYLLIHGTADDNVHFQQSAQ
DPRP1   768  WIFYDTGYTERYMGHPDONEGYYLGSVAMQAEKFPSEPNRLLLLHGFLDENVHFAHTSI
DPRP2   759  WMAYDTGYTERYMDVPENNQHGYEAGSVALHVEKLPNEPNRLLIIHGFLDENVHFAHTSI
DPRP3   680  LKLYASAFSERYIGMPSKEES..TYQEASVIHNVHGLKEENILIIHGTADTKVHFQHSAE

DPP4    719  ISKALVDVGVDEQAMWYTDEDHGIASSTAHQHIYTHMSHFIKQCFSLP..........
DPRP1   828  LLSFLVRAGKPYDLQIYPQERHSIRVPESGEHYELHLLHYLQENLGSRIAALKVI.....
DPRP2   819  LVSQLIRAGKPYQLQIYPNERHSIRCPESGEHYEVTLLHFLQEYL...........
DPRP3   738  LIKHLIKAGVNYTMQVYPDEGHNVSEK.SKYHLYSTILKFFSDCLKEEISVLPQEPEEDE
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FIG. 1B